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ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: LIQUID ANTIMICROBIAL COMPOSITIONS

(57) Abstract: ABSTRACT LIQUID ANTIMICROBIAL COMPOSITIONS A liquid antimicrobial composition comprises:(1) a mixture of iodide anions and thiocyanate anions;(2) periodic acid or an alkali metal salt thereof; and(3) optionally, a peroxidase. The composition may be used as a microbicide, disinfectant or for suppressing or killing viruses or spores.

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Liquid Antimicrobial Compositions

This invention relates to an antimicrobial composition comprising iodide and thiocyanate anions.

5

Particular compositions of this type are disclosed in WO-A-91/11105. These compositions comprise

- (1) iodide and thiocyanate anions in a weight:weight ( $I^-:SCN^-$ ) ratio of 0.1:1 to 50:1 and in a combined anion  
10 weight concentration of at least 5mg/kg;
- (2) D-glucose in a weight concentration of at least 0.2g/kg;
- (3) glucose oxidase as an oxidoreductase enzyme; and
- (4) optionally, a peroxidase, especially  
15 lactoperoxidase.

Preferred such compositions of WO-A-91/11105 are preservative compositions in a solid (dry powder), or liquid two-pack, form in which one pack contains the D-  
20 glucose and the other the glucose oxidase. The contents of the two packs are mixed and immediately used.

On the other hand WO-A-95/26137 describes antimicrobial compositions containing the same components as those of  
25 WO-A-91/11105 and preferably in the same proportions. However, WO-A-95/26137 does not recommend the immediate use of components mixed together; rather, it teaches the provision of an incubation period of from 12 - 48 hours before use. From this, it is clear that in order to  
30 achieve an antimicrobial effect using such compositions, it is necessary to allow the components to react with one

another to form a reaction product which then has the desired rapid antimicrobial activity.

As an alternative to compositions containing iodide and  
5 thiocyanate anions, antimicrobial compositions are known which are based on periodic acid, which is a known oxidising agent and electron acceptor. For example, DE-A-4301277 describes the use of periodic and/or  
10 orthoperiodic acid for the sterilisation of containers for storage and transportation of milk by treating the internal surfaces of the container at room temperature for 2 - 20 seconds with an aqueous solution of 0.1 to 5 wt% of periodic or orthoperiodic acid.

15 EP-A-0726357 describes a process for inhibiting the production and accumulation of volatile fatty acids by hydrolytic fermentative bacteria in an anionic pulp and paper processing stream in which the presence of hydrogen is monitored and at least one of a biocide and an  
20 electron acceptor is added. The use of sodium (para) periodate is recommended for the case where the presence of an electron acceptor and some inhibition of the microorganisms is required.

25 We have now found surprisingly that if, in an antimicrobial composition containing iodide and thiocyanate ions, D-glucose and glucose oxidase (such as a composition described in WO-A-91/11105 or WO-A-95/26137), the D-glucose and glucose oxidase in  
30 combination are replaced solely by periodic acid or an alkali metal salt thereof, an efficient liquid antimicrobial composition is obtained, which is capable

of having a rapid killing effect upon the microorganisms which it is used to treat.

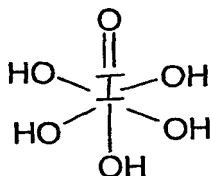
Thus, according to one aspect, the invention provides a  
5 liquid antimicrobial composition comprising

(1) a mixture of iodide anions and thiocyanate anions;

(2) periodic acid or an alkali metal salt thereof;  
and

10 (3) optionally, a peroxidase.

Periodic acid [CAS RN 10450-60-9], sometimes referred to an orthoperiodic acid, has the formula



15 Preferably, the periodic acid or salt thereof is present in the composition in an amount of from 25 to 500 ppm, more preferably from 200 to 500 ppm, by weight of the total weight of the composition.

20 Thus, even a composition containing as low an amount of periodic acid as 25 - 50 ppm can kill bacteria such as E.coli but for a broad spectrum of activity, the minimum amount should be about 100 ppm. Moreover, for a stable shelf life, at least 200 ppm is preferred. The preferred  
25 maximum amount is about 500 ppm.

Such compositions react considerably faster than the composition disclosed in WO-A-91/11105 and WO-A-95/26137

so that, instead of the 4 - 48 hours recommended for optimum potency, compositions embodying the invention may achieve a rapid kill of microorganisms immediately after mixing.

5

In contrast to the two-pack forms disclosed in WO-A-91/11105 and WO-A-95/26137 for use as a preservative, a liquid composition embodying the invention can be used as a disinfectant, in the form of a single, ready to use, product.

10

The spectrum of antimicrobial activity is also somewhat different from that of the abovementioned known compositions. In particular, compositions embodying the invention are particularly effective in combatting viruses and spores, e.g. bacillus spores.

15

The precise role played by the periodic acid in improving the antimicrobial efficiency of the iodide/thiocyanate anion system is not fully understood, although the mechanism seems to involve oxidation.

20

The pH of the composition may be from, say, 1 to 8 but is preferably less than 4.5 and, especially at low pH, the composition may contain free periodic acid. However, the composition may alternatively or additionally contain an alkali metal, especially the sodium, salt thereof.

25

As indicated above, the composition may additionally contain a peroxidase, especially lactoperoxidase; the presence of a peroxidase is surprisingly found to improve the shelf life of the composition. Thus, although this

30

might have been expected for an organic oxidation/reduction system as in WO-A-91/11105, it is surprising that such an effect is achievable with an inorganic system utilizing periodic acid.

5

Preferably the peroxidase is present in the composition in an amount of at least 10 U/kg.

10 In a composition embodying the invention, the weight:weight ratio of iodide:thiocyanate anions is preferably from 0.1:1 to 50:1, more preferably from 0.2:1 to 20:1 inclusive.

15 The iodide and thiocyanate anions are preferably present in the composition in a total amount of at least 5 mg/kg, based on the total weight of the composition. The iodide anions are preferably present in the composition at a weight concentration of at least 5 mg/kg, while the thiocyanate ions are preferably present at a weight  
20 concentration of at least 2 mg/kg, based on the total weight of the composition.

A composition embodying the invention may contain additionally a suitable carrier. Preferably, the carrier  
25 is water and the composition is an aqueous solution. However, the carrier may comprise water and, additionally, a surfactant or emulsifier, whereby the composition is an oil in water emulsifier or a surfactant based solution.

30

According to other aspects, the invention provides the use of a composition as defined above as a microbicide or

as a disinfectant respectively and especially the use of such a composition for suppressing or killing viruses or spores, e.g. bacillus spores.

- 5 In addition to the use of the composition as a microbicide or disinfectant, an anti-microbial composition embodying the invention may provide the active component in a wide variety of products which require potent antibacterial, anti-mould and/or anti-
- 10 yeast activities. Examples of such products include:
- a) deodorants e.g. for topical administration in the form of lotions;
  - 15 b) antibacterial skin washes e.g. in the forms of lotions;
  - c) anti-acne preparations e.g. in the form of lotions or creams;
  - 20 d) anti-athletes foot preparations e.g. in the form of lotions;
  - e) anti-dandruff preparations e.g. in the form of
  - 25 shampoos or lotions;
  - f) dental preparations, e.g. mouth washes suitable for general oral hygiene and, in particular, having anti-plaque properties, and dentrifices such as toothpastes,
  - 30 chewing gums and lozenges;

- g) impregnated materials e.g. wound dressings, sutures and dental floss;
- h) pharmaceuticals e.g. wound irrigants and burn treatments, anti-diarrhoeal agents and medicaments suitable for the treatment of infections such as Candida and Tinea infections;
- i) ophthalmic preparations e.g. eye washes and/or sterilising contact lenses; and
- j) sterilants e.g. for baby bottles and surgical or dental instruments.
- According to yet another aspect, the invention provides a method of killing or suppressing viruses or spores comprising contacting them within a composition as defined above.
- Embodiments of the invention will now be described in more detail with reference to the following Examples.

Example

- A composition contains
1. NaSCN 4.2 mg
  2. KI 7.3 mg
  3. Lactoperoxidase 70 international units
  4. Periodic acid 200 mg
  5. Water up to 100 ml.



Components 1 - 4 were added to 75 mls of distilled water and stirred until dissolved. The solution was then made up to 100 mls with distilled water.

- 5 The above solution was then immediately challenged with a  $1 \times 10^6$  cfu/ml inoculum of the following organisms.

Ps.aeruginosa NCIB 8626

S.aureus NCIB 9518

- 10 E.coli NCIB 8545

C.albicans ATCC 1023

A. niger ATCC 16404

- 15 Total kill of each of the above organisms was achieved in less than 5 mins.

Excellent anti-viral activity was also demonstrated against Echovirus 11 and Herpes simplex virus type 1 (HSV-1).

20

Excellent sporicidal activity was also demonstrated against B.cereus NCTC 2599 and B.subtilis NCTC 10073.

- 25 The solution was still demonstrating the above activity after six months storage at room temperature.

Claims

1. A liquid antimicrobial composition comprising:
  - (1) a mixture of iodide anions and thiocyanate anions;
  - (2) periodic acid or an alkali metal salt thereof; and
  - (3) optionally, a peroxidase.
2. A composition according to claim 1, wherein the periodic acid or salt thereof is present in the composition in an amount of from 25 to 500 ppm by weight of the total weight of the composition.
3. A composition according to claim 2, wherein the periodic acid or salt thereof is present in an amount of from 200 to 500 ppm by weight of the total weight of the composition.
4. A composition according to any preceding claim, wherein the weight:weight ratio of iodide:thiocyanate anions is from 0.1:1 to 50:1 inclusive.
5. A composition according to claim 4, wherein the weight:weight ratio of iodide:thiocyanate anions is from 0.2:1 to 20:1 inclusive.
6. A composition according to any preceding claim, wherein the iodide and thiocyanate anions are present in the composition in a total weight of at least 5 mg/kg, based on the total weight of the composition.

7. A composition according to any preceding claim,  
wherein the iodide anions are present in the composition  
to a weight concentration of at least 5 mg/kg and the  
thiocyanate ions to a weight concentration of at least 2  
5 mg/kg, based on the total weight of the composition.
8. A composition according to any preceding claim,  
which contains a peroxidase.
- 10 9. A composition according to claim 8, wherein the  
peroxidase is lactoperoxidase.
10. A composition according to claim 8 or claim 9,  
wherein the peroxidase is present in the composition in  
15 an amount of at least 10 U/kg.
11. A composition according to any preceding claim which  
additionally contains a suitable carrier.
- 20 12. A composition according to claim 11, wherein the  
carrier is water and the composition is an aqueous  
solution.
- 25 13. A composition according to claim 12, wherein the  
carrier additionally comprises a surfactant or emulsifier  
and the composition is an oil in water emulsifier or a  
surfactant based solution.
- 30 14. Use of a composition according to any preceding  
claim as a microbicide.

15. Use of a composition according to any one of claims  
1 to 13 as a disinfectant.

16. Use of a composition according to any one of claim 1  
5 to 14 for suppressing or killing viruses or spores.

17. A method of killing or suppressing viruses or spores  
comprising contacting them with a composition according  
to any one of claims 1 to 13.

# INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/GB 02/00025

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01N59/24 A01N59/12 A61L2/18 A61K33/40 A61K33/18  
/(A01N59/24, 59:12)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 26137 A (BOOTS CO PLC ;ASHWORTH DAVID WILSON (GB); GUTHRIE WALTER GRAHAM (G) 5 October 1995 (1995-10-05) cited in the application page 1, line 6-21 page 4, line 8 -page 5, line 10 -----	1-17
A	WO 91 11105 A (BOOTS CO PLC) 8 August 1991 (1991-08-08) cited in the application page 1, line 10 -page 2, line 24 page 5, line 31 -page 6, line 27 page 6, line 28 -page 7, line 20 -----	1-17
A	DE 43 01 277 A (STUBINITZKY HEINZ GUENTER) 14 July 1994 (1994-07-14) cited in the application column 1, line 50-55; claims 1,5 -----	1-17

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Information on patent family members

International Application No  
PCT/GB 02/00025

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9526137	A	05-10-1995	AU 697046 B2 AU 2110395 A CA 2186531 A1 WO 9526137 A1 EP 0752815 A1 IL 113070 A NZ 283139 A ZA 9502363 A	24-09-1998 17-10-1995 05-10-1995 05-10-1995 15-01-1997 28-10-1999 24-09-1998 26-09-1995
WO 9111105	A	08-08-1991	CA 2073768 A1 AT 110520 T AU 642467 B2 AU 7210191 A BG 96716 A DE 69103745 D1 WO 9111105 A1 EP 0514417 A1 ES 2059117 T3 IL 97112 A JP 2873084 B2 JP 5504567 T BG 61246 B1 BR 9105930 A DK 514417 T3 FI 923252 A IE 910157 A1 NO 300352 B1 NZ 236990 A US 5607681 A ZA 9100763 A	31-07-1992 15-09-1994 21-10-1993 21-08-1991 30-06-1994 06-10-1994 08-08-1991 25-11-1992 01-11-1994 07-10-1994 24-03-1999 15-07-1993 30-04-1997 10-11-1992 03-10-1994 15-07-1992 14-08-1991 20-05-1997 25-02-1993 04-03-1997 26-02-1992
DE 4301277	A	14-07-1994	DE 4301277 A1	14-07-1994